



IN THE UNITED STATES PATENT OFFICE

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Applicants: Bodo Junge  
Serial No.: 936,280  
Filed: August 23, 1978  
For: NEW 3,4,5-TRIHYDROXYPIPERIDINE COMPOUNDS, THEIR  
PRODUCTION AND THEIR MEDICAL USE  
Group No.: 121  
Examiner: R. A. Schwartz

DECLARATION

WALTER PULS declares:

He is an applicant in the above-identified application.

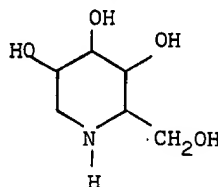
He was awarded the degree of Dr. med. in 1954 at the Medizinische Akademie of Düsseldorf, Germany.

Since 1956 he has been employed by Bayer AG, assignee of the above-identified application, in the field of physiological chemistry.

He is presently responsible for the evaluation of drugs for the treatment of diabetes, obesity and hyperlipemia at Bayer's Institute for Pharmacology at Wuppertal-Elberfeld.

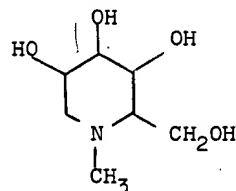
Under his supervision and direction tests were carried out to compare the blood glucose reducing properties of certain compounds enumerated below.

I. Compound of the formula



2-hydroxymethyl-3,4,5-trihydroxypiperidine ( $\pm$  1-desoxynojirimycin according to US Patent Specification 4,065,562.

II. Compound of the formula



N-methyl-2-hydroxymethyl-3,4,5-trihydroxypiperidine according to US Patent Application Serial No. 936,280.

The inhibition of the increase of glucose in the blood of rats after administration of boiled wheat starch with compound I and compound II respectively was determined according to the following table.

Table: Concentration of glucose in blood (mg/dl $\pm$  SD) of 6 sober rats in each test at various times after oral application of physiological sodium chloride solution (control, NaCl), or 1 g of boiled wheat starch (control starch)  $\pm$  compound I or compound II respectively.

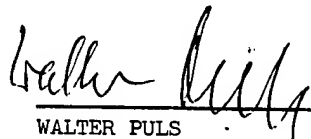
dose/kg per os	15	30	45	60 min.
control, NaCl	55 $\pm$ 5.2	57 $\pm$ 4.5	69 $\pm$ 4.9	66 $\pm$ 6.5
control, starch	127 $\pm$ 5.2	85 $\pm$ 17	95 $\pm$ 11	85 $\pm$ 13
2 mg of I in starch	123 $\pm$ 13	100 $\pm$ 19	86 $\pm$ 12	87 $\pm$ 10
4 mg of I in starch	110 $\pm$ 10	85 $\pm$ 11	94 $\pm$ 7.2	89 $\pm$ 15
8 mg of I in starch	88 $\pm$ 18 =====	89 $\pm$ 22	90 $\pm$ 9.9	82 $\pm$ 14

dose/kg per OS	10	20	30	45 min
control, NaCl	<u>64±8.4</u> =====	<u>53±3.9</u> =====	<u>66±8.2</u> =====	<u>55±3.8</u> =====
control, Starch	<u>108±7.7</u> =====	<u>110±2.4</u> =====	<u>90±1.8</u> =====	<u>61±6.3</u> =====
1 mg of II in starch	<u>66±9.5</u> =====	<u>68±7.8</u> =====	<u>80±6.9</u> =====	<u>87±1.3</u> =====
2 mg of II in starch	<u>65±5.8</u> =====	<u>61±6.7</u> =====	<u>64±5.9</u> =====	<u>63±5.8</u> =====
4 mg of II in starch	<u>60±1.6</u> =====	<u>59±2.9</u> =====	<u>62±3.1</u> =====	<u>58±3.3</u> =====

--- P < 0.05    — P < 0.01    === P < 0.001 compared with control, starch

As can be seen from the table compound II shows inhibition of the increase of glucose with low doses up to 45 minutes whereas compound I shows some inhibitory properties only during the first 15 minutes and only with much higher doses.

The undersigned declarant declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like to made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

  
WALTER PULS

Dated: 19. Mai 1979